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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,880	12/12/2003	John P. Fruehauf	02-1270-A	1031

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EXAMINER	
YAO, LEI	
ART UNIT	PAPER NUMBER
1642	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/734,880	FRUEHAUF, JOHN P.	
	Examiner	Art Unit	
	LEI YAO	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *1-19 and 22-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20, 21, and 40-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Arguments and Amendments

The Amendment filed on 4/28/08 in response to the previous Non-Final Office Action (12/27/2007 is acknowledged and has been entered.

Claims 1-43 are pending.

Claims 1-19, 22-39 have been withdrawn for non-elected invention.

Claims 20, 21, and 40-43, drawn to amethod for identifying a tumor resistant to taxane drugs by determining the gene expression of one or plurality of genes, are under consideration.

Rejections Withdrawn

1. The rejection of claims 20, 21, and 40-43 rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it is not clear how the claimed invention can be achieved by method steps recited in the claims is withdrawn in view the clarification by Applicant, who indicated that the claimed invention is drawn to a method of identifying a tumor or identifying a tumor resistance to taxane comprising detecting the differential expression of one or a plurality of genes between the tumor cell and non-tumor cell within the tissues in the remarks (page 12, line 2-3 from bottom). The new art rejections are also applied below according to this clarifications.

2. The rejection of claims 20, 21, 40-44 under 35 U.S.C. 102(b) as being anticipated by Mechetner et al., is withdrawn in view the amendment to delete the ATPase in the claims 20 and 42 and Applicant's argument.

3. The rejection of claims 20. 21 40-44 under 35 U.S.C. 102(b) as being anticipated by Junkun et al., are withdrawn in view of Applicant's argument that the claims are interpreted as identifying tumor or tumor cells that are resistant to taxane chemotherapeutic drugs (page 15, para 3).

Response to Arguments and Rejection Maintained

35 U.S.C. 112 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 20, 21, and 40-43 remain rejected under 35 U.S.C. 112, first paragraph, New Matter as the following:

It is noted that the claims as newly amended claims reciting GenBank numbers in the independent claims 20, 40, 42, and 43 are not supported by the specification. Instant specification as filed, although provides a list of names of altered gene expression in the chemotherapeutic drug resistant cells compared to the sensitive cells, does not provide sufficient support for the relationship of the names of genes associated with the GenBank Accession Nos recited in the amended claims.

Applicant does not argue the new matter rejection and does not point out the support in the specification, therefore the rejection is maintained as set forth above.

Written Description

Claims 20, 21, 40-43 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which is not possessed by Applicant as the following:

Claims are drawn to accession Nos from public databases: GenBank Accession No. AF458589, GenBank Accession No. U79283, GenBank Accession No. BC063851, GenBank Accession No. AY194849, GenBank Accession No. D00099, GenBank Accession No. L34673, GenBank Accession No. AF060181, GenBank Accession No. AF237631.

Claims are drawn to sequences incorporated by reference to an accession no. from a public database, and for which no structural identity is provided by nucleotide or amino acid sequence in the specification at the time of filing. One skilled in the art cannot determine from the written disclosure of the specification alone whether the sequence as claimed is identical to the sequence contained in the database under the accession no. at the time the application was filed.

One skilled in the art could not determine based on the accession no. alone which entry for a sequence was being claimed, if the sequence entry was modified or revised after the time of application filing. Further, because multiple sequence entries could have been made after the

filing date, then any post-filing date sequences would raise an issue of new matter. Thus one skilled in the art would conclude that Applicants were not in possession of any of the claimed sequences referred to by accession no. based on the written disclosure in the specification alone.

The response filed 4/28/2008 has been carefully considered but is deemed not to be persuasive. The response states:

> Applicants submit that the GenBank Accession Nos for all of the genes recited in the claims were available at a public database (as also acknowledged by the Office in the Action) and were, therefore, part of the general knowledge in the art at the time of filing of the application.
>
> Applicants submit Exhibit 1 showing gene sequence revision history that is available on the GenBank public database…. As is evident from the Exhibit, the dates at which the sequences were first seen on the public database for all GenBank Accession Nos corresponding to the recited genes were before the filing date of the current application. Consequently, the relationship between the listed genes and the GenBank Accession Nos was part of the public knowledge and one of skill in the art.
>
> Furthermore, each of the GenBank Accession Nos corresponded to only one sequence. Thus, one of skill in the art would have understood that the sequence recited in the claim (but, it is important to realize, not itself being claimed) is the sequence disclosed on the public database at the time of filing. Additionally, for the genes that have a second version of the gene sequence submitted after the filing of current application, the second version sequence is 100% identical to the first version of the sequence. Thus, one of skill in the art could easily determine which entry for a sequence was being claimed by the Applicants.

In response, first, as set forth in the rejection, the GenBank Accession No could change in time and the Office could not determine that the sequence as claimed is identical to the sequence contained in the database under the Accession No. at the time the application was filed. For example, urokinase receptor (AY194849), was first seen at NCBI on Dec 21, 2002, the date after filing the priority application 60432922 dated Dec 12, /2002. Furthermore, the zinc finger protein (AP060181, claim 20) does not exist with the accession No in the protein and nucleotide database. Second, as the revision history provided by applicant (exhibit 1) showing the revision history of each accession number, many of the accession Nos are revised many times after filing the instant application and the Office could not determine which revision is used at the time

of filing the application and not know the sequence in which revision is referred at the time of examining the application. Although some of the revised sequences are the same or identical as previous version, the additional information or correction might be added in the revised version, which could affect the use of the sequence in the claimed method or public opinion (one skilled in the art) to use the gene or gene product, which would also result in an effect on the examination of the claimed invention. Thus, Applicant's argument has not been found persuasive, and the rejection is maintained for reason of the records.

Applicant is also invited to provide declaration to provide evidence and statement indicating that each of the sequences corresponding to the GenBank Accession No recited in the claims has not been changed before and after filing date of the instant application.

The following is a New Ground of rejection based on new consideration

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 20, 21, and 40-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as

routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The instant claims, as written, are drawn to a method for 1) identifying a breast tumor that is resistant to a taxane chemotherapeutic drug comprising the steps of: determining, comparing the gene expression levels of one and/or plurality of genes in a tumor sample or tumor cells and the non-tumor cells, and then to identify a taxane resistant tumor or tumor cells. Thus, the invention claims a method of identifying the taxane resistant tumor or taxane resistant tumor cell by determining the differential expression of genes between the tumor (tumor cell) and normal tissue (normal cell).

To satisfy the requirement of 112, 1st paragraph, it is necessary that the specification provide an enabling disclosure of how to make and use a claimed invention. The objective of the claims is method of identifying the taxane resistant breast tumor (or cell) by determining the differential expression of one of more genes between the breast tumor cell and normal breast cell. Thus, it would be expected that one of skill in the art would be able to do so without undue a quantity of experimentations.

The specification teaches intrinsic gene expression in taxane sensitive vs resistant breast tumor (table I), induced gene expression by taxane sensitive vs resistant breast tumor (table II), and overlapping the gene sets for the sensitive vs resistant and endothelial cells (table III). Thus, the application provides a teaching on the gene expressions between the sensitive

and resistant tumor and claims a method of identifying the taxane resistant tumor (cell) by comparing the gene expression in tumor to the normal tissue or cell.

One cannot extrapolate the teachings of the specification to the scope of the claims because the specification does not provide teaching or direction/guideline or any objective evidence to show that the taxane resistant tumor or cell could be identified by comparing the differential expression of the genes between the tumor cell and non-tumor cell that has never been exposed to the taxane chemotherapeutic drugs.

It is known in the field of breast cancer therapy that the resistant tumor or tumor cell are developed during and after the patient are administered with taxane drug in vivo or the cell are exposed to taxane drugs in vitro. The artisans often measure and compare the differential gene expression between the resistant and sensitive tumor (cell) to determine whether the tumors or tumor cells are resistant to the taxane drug. For example, a multi-drug resistant protein, p-glycoprotein (Pgp) is expressed when the tumor cells exposed to the toxol (a taxane drug) (Mechetner et al., abststract, clinical cancer research, vol 4, page 389-398, 1998, provided 12/2007) and Pgp is not expressed in the tumor that has never been exposed to the such drug. Thus, the expression of Pgp can be used for determining whether the tumor is taxane resistant. The instant specification also provides the same teaching for identifying the expression of specific genes listed in table I-III. Neither the art of record nor specification have provided any teaching to determine the taxane resistant breast tumor or cells by comparing the expression between tumor and non-tumor when the tumor has not been exposed to any taxane drug. According, the specification provides a non-enabled disclosure and no objective evidence for claimed invention drawn to a method of identifying a taxane resistant tumor or taxane resistant cells from a tumor by comparing the expression of one or more of the genes listed in the claims between the tumor and non-tumor cells, which are not exposed to a taxane drug.

In view of the absence of objective evidence and lack of direction/guideline, experimentations, and the unpredictability of expressing the genes listed in the claims wherein the tumor or tumor cells have not been exposed to a taxane drug, one skilled in the art would be forced into undue experimentation to practice the claimed invention for identifying a taxane resistant tumors or cell within the tumors.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao, Ph.D./
Examiner, Art Unit 1642

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643